

V. CLAIMS

What is claimed is:

1. An isolated molecular complex comprising a proteoglycan and an isolated receptor protein for a myelin-derived-growth-inhibitory protein or a fragment thereof, wherein the receptor protein has a proteoglycan binding domain.
2. An isolated molecular complex of claim 1, wherein the myelin-derived-growth-inhibitory protein is selected from the group consisting of Nogo, MAG, and OMgp.
3. The isolated molecular complex of claim 1, wherein the proteoglycan is a heparan sulfate bearing proteoglycan.
4. The isolated molecular complex of claim 3, wherein the heparan sulfate is heparin.
5. The isolated molecular complex of claim 1, wherein the receptor protein is NgR1.
6. The isolated molecular complex of claim 1, wherein the receptor protein is NgR3.
7. A method of modulating neurite outgrowth comprising the step of contacting a neuron with an effective amount of the isolated receptor protein for a myelin-derived-growth-inhibitory protein comprising an amino acid sequence having less than 74% sequence homology to the amino acid sequence of SEQ ID NO:1, wherein the isolated receptor protein is contacted with a proteoglycan.
8. A method of modulating neurite outgrowth comprising the step of contacting a neuron with an effective amount of a glycosaminoglycan that binds an isolated receptor protein for a myelin-derived-growth-inhibitory protein comprising an amino acid sequence having less than 74% sequence homology to the amino acid sequence of SEQ ID NO:1.
9. A method of modulating neurite outgrowth comprising the step of contacting a neuron with an effective amount of a glycosaminoglycan that modulates binding of proteoglycans with an isolated receptor protein for a myelin-derived-growth-inhibitory protein comprising an amino acid sequence having less than 74% sequence homology to the amino acid sequence of SEQ ID NO:1.
10. A method of modulating neurite outgrowth comprising the step of contacting a neuron with an agent that promotes or prevents sialic acid binding to a receptor for a myelin-derived-growth-inhibitory protein.
11. A method of treating a central nervous system disorder in a subject comprising administering to the subject an effective amount of an isolated receptor protein for a myelin-derived-growth-inhibitory protein comprising an amino acid sequence having less than 74% sequence homology to the amino acid sequence of SEQ ID NO:1.
12. The method of claim 11, further comprising administering an effective amount of a proteoglycan to the subject.
13. A method of treating a central nervous system disorder in a subject comprising

administering to the subject an effective amount of a glycosaminoglycan that binds an isolated receptor for a myelin-derived-growth-inhibitory protein, wherein the isolated receptor protein comprises a domain with lectin activity.

- 5 14. A method treating a central nervous system disorder in a subject comprising administering to the subject an effective amount of a glycosaminoglycan that modulates binding of proteoglycans with an isolated receptor for a myelin-derived-growth-inhibitory protein, wherein the isolated receptor protein comprises a domain with lectin activity.
- 10 15. A method of treating a central nervous system disorder in a subject comprising administering to the subject an effective amount of an agent that promotes or prevents sialic acid binding to a receptor for a myelin-derived-growth-inhibitory protein.
- 15 16. A method of modulating neurite outgrowth comprising contacting a myelin-derived-growth-inhibitory protein with a first receptor for a myelin-derived-growth-inhibitory protein and a second receptor for a myelin-derived-growth-inhibitory protein.
- 20 17. The method of claim 16, wherein the first receptor is NgR1 and the second receptor is NgR2.
18. The method of claim 16, wherein the first receptor is NgR1 and the second receptor is NgR3.
- 25 19. The method of claim 16, wherein the first receptor is NgR2 and the second receptor is NgR3.
20. The method of claim 16, further comprising a third receptor for a myelin-derived-growth-inhibitory protein.
- 30 21. The method of claim 20, wherein the first receptor is NgR1, the second receptor is NgR2, and the third receptor is NgR3.
22. A method of identifying a compound that inhibits the binding of myelin-derived-growth-inhibitory protein to two or more myelin-derived-growth-inhibitory protein receptors, the method comprising:
- 35 a. providing two or more polypeptides comprising the ligand-binding domain of myelin-derived-growth-inhibitory protein receptors, but lacking the GPI anchor domain of myelin-derived-growth-inhibitory protein receptors;
- 40 b. contacting the polypeptides with myelin-derived-growth-inhibitory protein and a test compound; and
- 45 c. determining whether binding of a myelin-derived-growth-inhibitory protein to the polypeptides is decreased in the presence of the test compound, a decrease in said binding being an indication that the test compound inhibits the binding of myelin-derived-growth-inhibitory protein to the myelin-derived-growth-inhibitory protein receptors.
- 50 23. A chimeric protein comprising a ligand binding domain of NgR1 and a unique domain of NgR2.

24. The chimera of claim 23, wherein the chimera comprises amino acids 1-377 of NgR1 and 353-420 of NgR2.

5 25. The chimera of claim 23, wherein the chimera comprises amino acids 1-346 of NgR1 and 328-420 of NgR2.

26. The chimera of claim 23, wherein the chimera comprises amino acids 1-346 of NgR1 and 328-473 of NgR2.

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27. The chimera of claim 26, wherein the chimera comprises SEQ ID NO: 19.

28. The chimera of claim 23, wherein the chimera comprises amino acids 1-314 of NgR1 and 315-420 of NgR2.

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29. The chimera of claim 28, wherein the chimera comprises SEQ ID NO: 13.

30. A chimeric protein comprising a ligand binding domain of NgR2 and a unique domain of NgR1.

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31. The chimera of claim 30, wherein the chimera comprises amino acids 1-352 of NgR2 and 378-473 of NgR1.

32. The chimera of claim 30, wherein the chimera comprises amino acids 1-327 of NgR2 and 349-473 of NgR1.

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33. The chimera of claim 32, wherein the chimera comprises SEQ ID NO: 17.

34. The chimera of claim 32, wherein the chimera comprises amino acids 1-315 of NgR2 and 314-473 of NgR1.

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35. The chimera of claim 34, wherein the chimera comprises SEQ ID NO: 11.

36. A chimeric protein comprising a ligand binding domain of NgR3 and a unique domain of NgR2.

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37. The chimera of claim 36, wherein the chimera comprises SEQ ID NO: 15.

38. A chimeric NgR1 protein comprising the MAG binding motif of NgR2.

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39. The chimeric protein of claim 38, wherein the chimera comprises amino acids 1-314 of NgR1 and 315-327 of NgR2, and 354-473 of NgR1.

40. The chimera of claim 38, wherein the chimera comprises SEQ ID NO: 21.

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41. The chimera of claim 38, wherein the chimera is soluble.

42. A nucleic acid encoding the protein chimera of claim 23.

43. A nucleic acid encoding the protein chimera of claim 30.

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44. A nucleic acid encoding the protein chimera of claim 37.

45. A nucleic acid encoding the protein chimera of claim 38.

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46. A method of inhibiting MAG-NgR2 complex formation comprising contacting the complex with an agent that disrupts sialic acid dependent binding to a receptor for a myelin-derived-growth-inhibitory protein.

10 47. The method of claim 46, wherein the agent is *Vibrio cholerae* neurominidase.

48. The method of claim 46, wherein the agent is tunciamycin.

49. The method of claim 46, wherein the agent is ganglioside GT1b.

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50. A method of modulating myelin inhibitor activity comprising contacting a myelin-derived-growth-inhibitory protein with the chimera of claim 38.

20 51. A method of treating a central nervous system disorder in a subject comprising administering to the subject an effective amount of the chimera of claim 38.

52. An isolated molecular complex comprising a first isolated receptor protein for a myelin-derived-growth-inhibitory protein or fragment thereof and a second isolated receptor protein for a myelin-derived-growth-inhibitory protein or fragment thereof.

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52. The isolated molecular complex of claim 52, wherein the first isolated receptor protein is NgR1.

30 53. The isolated molecular complex of claim 52, wherein the second isolated receptor protein is NgR2.

35 54. An isolated molecular complex comprising proteoglycan, an isolated receptor protein for a myelin-derived-growth-inhibitory protein or fragment thereof, and a fibroblast growth factor (FGF).

55. The isolated complex of claim 55, wherein the proteoglycan is a herparan sulfate bearing proteoglycan.

40 54. The isolated complex of claim 56, wherein the herparan sulfate bearing proteoglycan is syndecan-3.

56. The isolated complex of claim 55, wherein the myelin-derived-growth-inhibitory protein is selected from the group consisting of Nogo, MAG, and OMgp.

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57. The isolated complex of claim 55, wherein the FGF is FGF1.

58. The isolated complex of claim 55, wherein the FGF is FGF2.

50 59. The isolated complex of claim 55, wherein the FGF is FGF3.

60. The isolated complex of claim 55, wherein the FGF is FGF4.

61. The isolated complex of claim 55, wherein the receptor protein is NgR1.

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61. The isolated complex of claim 55, wherein the receptor protein is NgR1 .